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Thymic B-Cell Non-Hodgkin's Lymphoma in a Child

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A 13-year-old male developed thymic non-Hodgkin's lymphoma. Microscopically, the tumor was composed of large cells, resembling centroblasts. Immunohistochemically, the tumor demonstrated leukocyte common antigen$^+$, L26 (B-cell)$^+$, UCHL1 (T-cell)$^-$, suggesting the B-cell phenotype. In contrast to the terminally differentiated phenotype (CD10$^-$, surface immunoglobulin$^-$) observed in adult cases, flow cytometric analysis showed that they were relatively immature: CD10$^+$, CD19$^+$, HLA-DR$^-$, IgM$^{+/-}$, kappa$^+$. He was successfully treated with intensive chemotherapy. Since childhood thymic lymphomas are exclusively small non-cleaved cell lymphoma with T-cell phenotype, this case represents a unique entity in children. Am. J. Hematol. 57:48–50, 1998.

Key words: B-cell non-Hodgkin's lymphoma; thymus; child

INTRODUCTION

The anterior mediastinum is often found to be involved at presentation in children with lymphoma [1]. Of the non-Hodgkin's lymphoma (NHL), presenting mediastinal disease is most often seen with lymphoblastic lymphoma, primarily of the T-cell type [2]. However, within the past few years there have been several series of adult non-lymphoblastic NHL with prominent mediastinal involvement [3–7]. Clinical features of mediastinal large B-cell lymphoma appear to be a distinct clinicopathologic entity, with a median age in the fourth decade, a higher incidence in females than males, and a locally invasive anterior mediastinal mass originating in the thymus, with frequent airway compromise and superior vena cava syndrome [7]. Childhood cases have not been reported.

We report here that thymic B-cell NHL can be seen in a child and that the tumor represents a relatively immature immunophenotype of B-cell differentiation in contrast to the terminally differentiated B-cell phenotype in adults.

CASE REPORT

A 13-year-old male presented with a 2-month history of chest pain. He lost 8.5 kg weight in 2 months. He was admitted to the hospital in February 1991. On physical examination, there were several small lymph nodes in the neck. There was no anemia, bleeding tendency, or hepatosplenomegaly. Chest X-ray, CT scan, and MR imaging demonstrated an anterior mediastinal mass (Fig. 1A). Gallium-67 scintigraphy showed increased uptake at the primary mediastinal tumor. Angiography showed that the tumor was fed with the right internal mammary artery, suggesting the thymic origin of the tumor. Bone marrow aspiration, lumbar tap, and bone scan were normal. Laboratory findings included WBC 7.8×10^9/L, Hb 128 g/L, Platelet 406×10^9/L, lactic dehydrogenase 309 U/L, IgG 20.3 g/L, IgA 4.23 g/L, IgM 1.34 g/L. Abdominal and cranial CT scans were normal.

Percutaneous needle biopsy was not conclusive; thymic carcinoma could not be ruled out. He underwent resection of the anterior mediastinal mass (approximately 90% resection). Microscopically, the tumor is composed of large cells with variable nuclear features with pale cytoplasm, resembling centroblasts (Fig. 2A). The tumor contained Hassall's bodies, suggesting the thymic origin

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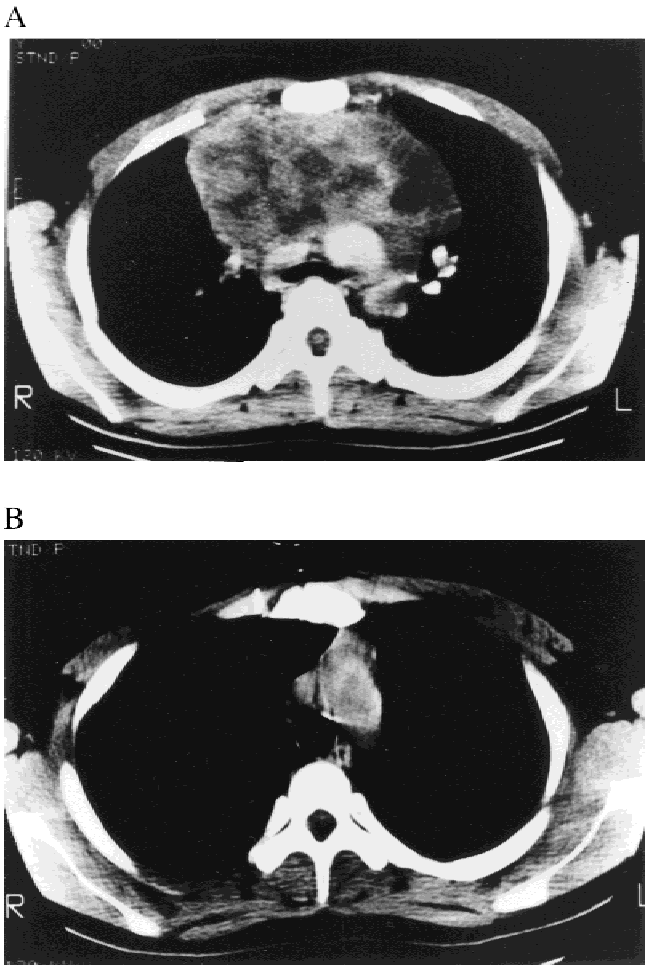

Fig. 1. CT scan of the chest. Pretreatment chest CT scan Demonstraing (A) anterior mediastinal tumor and (B) normal posttreatment chest CT scan.

of the tumor. Immunohistochemically, the specimen demonstrated leukocyte common antigen (LCA)$^+$, L26 (B-cell)$^+$, UCHL1 (T-cell)$^-$, Ber H2 (CD30)$^-$, epithelial membrane antigen$^-$, neuron-specific enolase$^-$, S100$^-$, lysozyme$^-$, suggesting the B-cell characteristics of the tumor (Fig. 2B,C). Flow cytometric analysis of single cell suspension of the tumor was done as previously described [8]. The results showed that they were relatively immature: CD45$^+$, CD10$^+$, CD19$^+$, HLA-DR$^-$, IgM$^{+/-}$, kappa$^+$ (Fig. 2D). Cytogenetic analysis yielded 44, x, −Y, −2, −21, i(7q), del(13)(q12q14), del(15)(q15), +der(2)t(2;?), +der(21)t(21;?)(p11;?). Collectively, the mediastinal tumor was B-cell non-Hodgkin's lymphoma (diffuse large cell; clinical stage III), which originated in the thymus.

A regimen of systemic chemotherapy (High Risk Lymphoma Protocol, Mie University) was successfully administered. After the patient received intensive chemotherapy, normalization of the chest CT scan was achieved (Fig. 1B). Chemotherapy was discontinued in August 1993. The patient remained in complete remission at the latest follow-up 57+ months after the initial diagnosis.

DISCUSSION

The mediastinum is known to be the primary site of lymphoblastic T-cell tumors, Hodgkin's disease, and thymic carcinoma [9]. Mediastinal mass in childhood NHL is most often seen with T-cell lymphoblastic lymphoma [2]. Nevertheless, there are few reports on primary NHL of the mediastinum with pronounced aggressiveness and poor prognosis. Yousem et al. have reported that 17 of 19 with mediastinal NHL (median age, 29 years) showed diffuse large cell; 37% of them showed prominent sclerosis; 6 of the cases showed evidence of immunoglobulin production with light chain restriction; 12 additional cases were shown to be of B-cell lineage but did not show evidence of immunoglobulin production [10]. Moller et al. reported eight primary mediastinal NHLs occurring in young adults (median age, 29.4 years), predominantly female (six of eight) adults. Most patients responded badly to aggressive therapy. No patient developed leukemia. The tumors were of diffuse large cell type or poorly differentiated lymphocytic. In all cases, the immunophenotype was CD10$^-$, CD19$^+$, CD20$^+$, CD21$^-$, immunoglobulin$^-$, and PC-1 (plasma cell)$^+$, suggesting a terminal B-cell differentiation [3]. Jacobson et al. have demonstrated that 30 adults (median, 34 years; male to female ratio, 1:2) with large cell lymphoma predominantly localized to the mediastinum [6]. In a revised European-American classification of lymphoid neoplasms, primary mediastinal large B-cell lymphoma was classified as large B-cell lymphoma subtype [7]. As compared with mediastinal T lymphoblastic lymphoma, which has pronounced male predominance (e.g., Brittinger et al. [11], ratio of males to females 9:1) large B-cell lymphoma of the mediastinum appears to be a distinct clinicopathologic entity, with a median age in the fourth decade, and a higher incidence in females than males [7].

B lymphocytes were found within the normal thymus medulla of normal thymuses of different ages (less than 1% of medullary lymphoid cells) [5]. Although the significance of B-cells in the thymic medulla is largely unknown, Hofmann et al. postulated that they contribute to tolerance induction to self-antigens of the B lymphocytes in the developing T-cell population [5].

The current case represents the unique thymic B-cell lymphoma: a male child with a relatively immature immunophenotype of B-cell differentiation and probably a good prognosis.

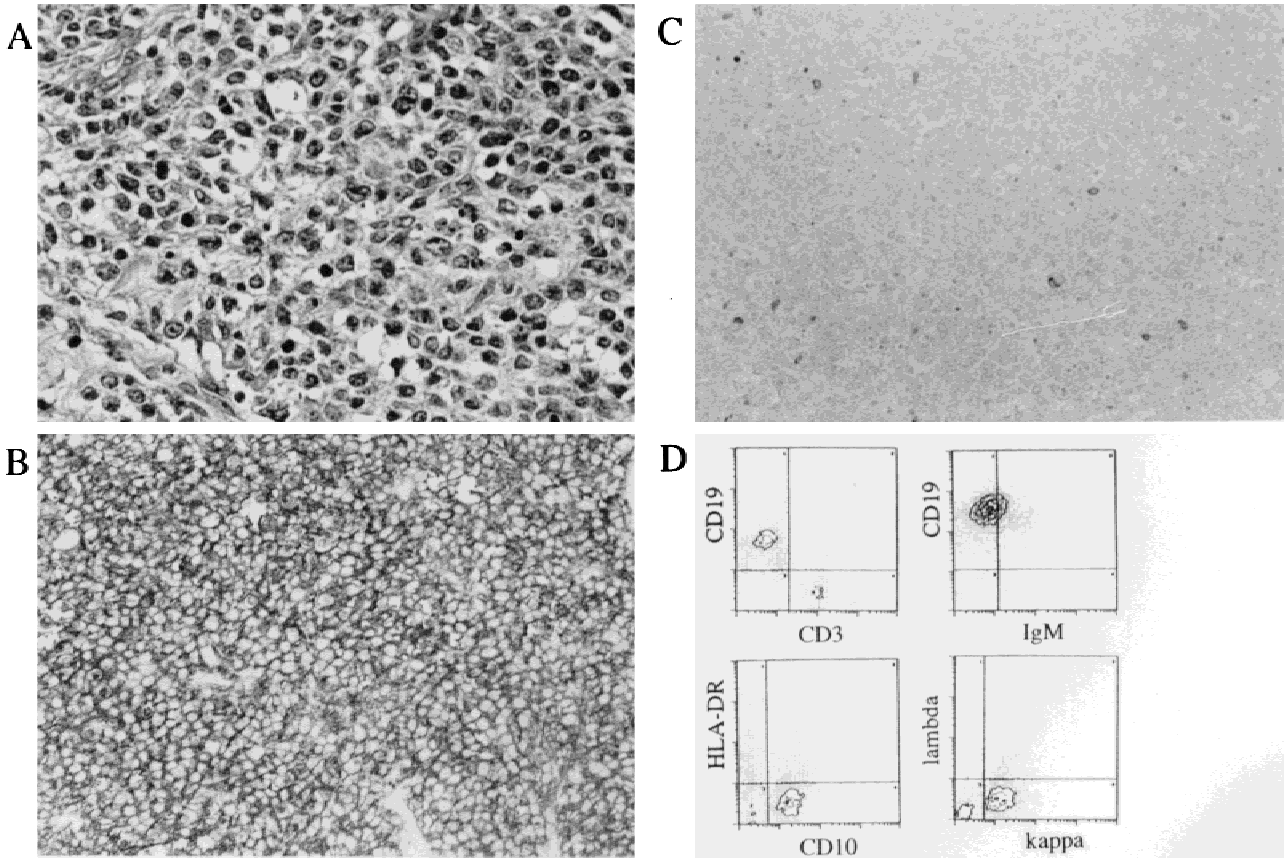

Fig. 2. Histology and immunophenotype. A: Histological appearance of mediastinal large cell lymphoma (H&E, ×500). B: The tumor is positive for L26 (B cell). C: The tumor is negative for T-cell antigen (UCHL1) (B and C, immunohistochemistry, ×250). D: Flow cytometric analysis of the tumor revealed that it represented CD10^{+}, CD19^{+}, HLA-DR-, IgM$^{-/+}$, kappa^{+} immunophenotype.

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